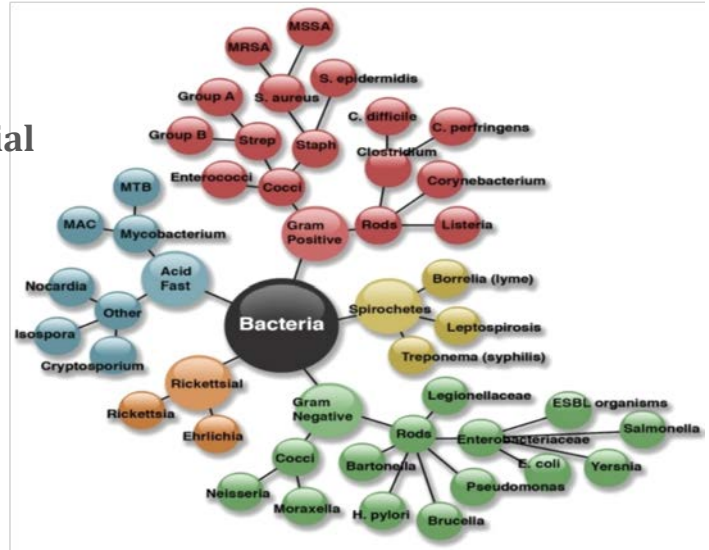
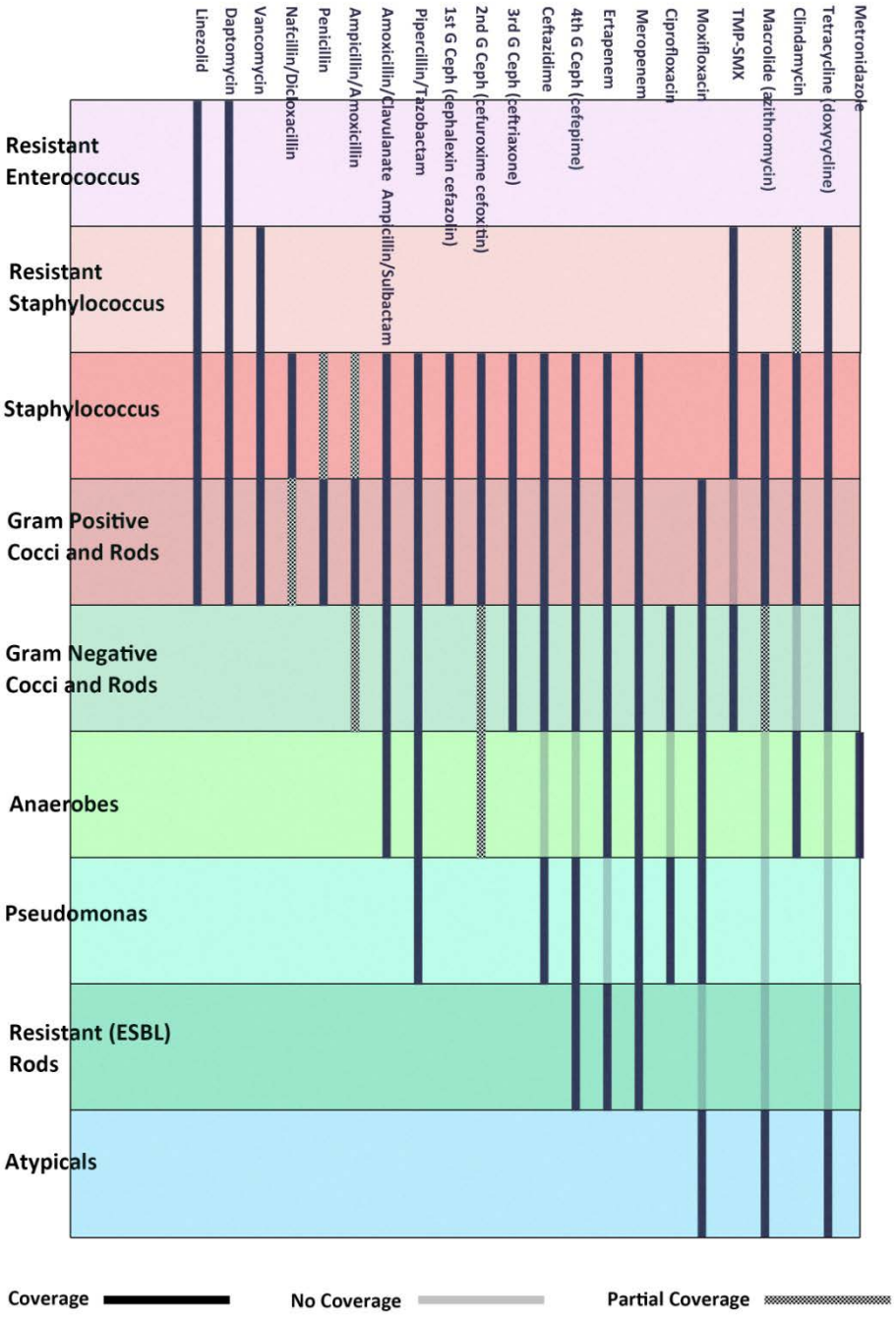
Anti-bacterial Primer





Penicillin

Penicillins active against many **gram positive cocci** including meningiococci, most streptococci including Group A, Group B, *S. viridans*, and *S. pneumoniae*, many **gram positive rods** including listeria, many **gram negative cocci** including *N. meningitides*, and *N. gonorrhoeae*., and many **spirochetes** including syphilis, leptospirosis, and *Borrelia*. Drug of choice for Group A, Group B, and syphilis. All PCNs associated with tubulo-interstitial nephritis, hemolytic anemia and Type I IgE mediated hypersensitivity reactions.

Semi-synthetic or narrow-spectrum penicillins (antistaphylococcal)

Semisynthetic penicillins like nafcillin, oxacillin, and dicloxacilin are primarily used against ***S. aureus*** (excepting resistant strains) because 85% have beta lactamase.

Extended-spectrum penicillins (amino-penicillin)

Extended-spectrum penicillins including ampicillin, amoxicillin, ampicillin-sulbactam, and amoxicillin-clavulanate are active against many **gram positive cocci**, many **gram positive rods**, and some **gram negative rods** including E. *coli, H. influenzae, Salmonella*, *Shigella*, and *Proteus*. Ampicillin is drug of choice for Listeria and enterococcus.

Antipseudomonal penicillins

Antipseudomonal penicillins including ticarcillin-clavulanate and piperacillin-tazobactam are active against many **gram positive cocci,** and better against **gram negative cocci, gram negative rods,** and **anaerobes**.

Carbapenems

Broad spectrum beta-lactamase antibiotics including ertapenem with activity against most **gram positive cocci**, most **gram positive rods**, most **gram negative cocci**, most **gram negative rods**, , and **ESBL-producing organisms** (including E. coli, Kelbsiella, Enterobacter and related genera). Does NOT cover *E faecium, B cepacia, Corynebacterium jeikeium, Stenotrophomonas maltophilia, Acinetobacter species*, and resistant staph. Ertapenem does not cover *Pseudomonas*. Carbapenems have a 5-15% cross-reactivity with penicillins (BMJ 2012; Ann Pharm 2009).

Antipseudomonal carbapenems

Broad spectrum beta-lactamase antibiotics including meropenem, imipenem, doripenem with activity against most **gram positive cocci**, most **gram positive rods**, most **gram negative cocci**, most **gram negative rods**, ***Pseudomonas species*** and **ESBL-producing organisms.** Imipenem can lower the seizure threshold.

1st Generation cephalosporins

1st generation cephalosporins including cefazolin are active against most **gram positive cocci** including staphylococci and streptococci. They have better coverage than amino penicillins against some **gram negative rods** including *E. coli, Klebsiella,* and *Proteus*. Best for skin and soft tissue infections. They have NO activity against enterococci and *Listeria*. First gen cephalosporins have a 10-15% cross reactivity/cross allerginicity with penicillins.

2nd Generation cephalosporins

2nd generation cephalosporins including cefoxitin are more active against gram negative organisms but less effective at gram positive organisms. Some are active against anerobes; cefoxitin is used primariy for abdominal/pelvic infections because of its anaerobic coverage.

3rd Generation cephalosporins

3rd generation cephalosporins are generally not degraded by beta-lactamase and are variably effective against **gram positive cocci**, especially effective against **gram negative cocci** including *N. gonorrhoeae*, and active against most **gram negative rods** including *E. coli, Klebsiella, Proteus, Enterobacter* and *Serriatia*. Ceftriaxone is drug of choice for PCN-resistant streptococcus and empiric treatment of meningitis (along with vancomycin and ampicillin).

3rd Generation antipseudomonal cephalosporins

Only some 3rd generation cephalosporins are active against ***Pseudomonas*** – especially ceftazidime.

4rd Generation cephalosporins

4th generation cephalosporins including cefepime are broad-spectrum with enhanced stability to cephalosproinases. They have the **gram positive activity** of 1st generation cephalosporins and **gram negative activity** of 3rd generation cephalosporins. They are especially effective against **extended spectrum beta-lactamase (ESBL) organisms**.

Aztreonam

Aztreonam is a monobactam that is good only against aerobic and facultative **gram-negative bacteria**. Spectrum similar to aminoglycosides and 3rd generation cephalosporins for gram-negative aerobes. Effective against ***Pseudomonas***. It is NOT effective against gram-positive cocci or anaerobes. Rarely associated with hepatotoxicity. There is no demonstrated cross-reactivity or cross allergenicity with penicillins

Oxazolidinones (linezolid)

Oxazolidinones block bacterial protein synthesis by binding a ribosomal subunit. Linezolid is active against **gram-positive organisms** including **methicilin-resistant *S. aureus*** and **vancomycin-resistant enterococci** and **anaerobes**. Excellent pulmonary and renal bioavailability. Associated with bone marrow suppression and optic neuropathy.

Fluoroquinolones

Fluoroquinolones are a set of wide-spectrum antibiotics that inhibit bacterial DNA synthesis. They are active against **gram negative aerobic organisms** including gram **negative rods** and ***Pseudomonas***. Ciprofloxacin has only intermediate activity against gram positive organisms. Fluoroquinolones have no activity against anaerobes. Quinolones can increase the effect of warfarin and cyclosporine. They are associated with retinal detachment, connective tissue problems including tendon rupture, and QT prolongation. Parenteral and oral forms have similar bioavailability.

Sulfonamides (trimethoprim-sulfamethoxazole)

The two drugs together create a synergistic blockade of bacterial folate synthesis. Active against **gram negative aerobic organisms** including gram negative rods and many **sporozoa** including ***Pneumocystis jirovici***. Tends to be the drug of choice for community acquired MRSA infections. TMP-SMX can increase warfarin bioavailability and decrease metabolism. Trimethoprim can cause cytopenias, hyperkalemia in settings of renal insufficiency, Stevens-Johnson, and can an increase creatinine *without* affecting renal clearance.

Macrolides

Effective against **gram positive cocci**, **gram negative cocci**, and **atypical organisms** including ***M. pneumonia***, ***C. pneumoniae***. Azithromycin has better coverage against ***H. influenza*** and ***S. pneumonia*** than erythromycin. Clarithromycin is associated with over 80 well-described drug interactions and should be avoided. All macrolides tend to increase warfarin activity and have been associated with QT prolongation.

Rifampin (rifamycin)

Rifampin is bacteriacidal with activity against **gram positive cocci**, **gram negative cocci**, and **acid-fast bacilli**. Never give this agent alone to treat an acute infection because organisms rapidly develop resistance to it.

Vancomycin

A glycopeptide with activity against most **gram positive organisms** including **methicillin-resistant staphylococci**, ***Clostridia***, and ***Corynebacterium***. Associated with "Red man syndrome", renal and ototoxicity. Renally cleared and must be dose adjusted in settings of renal insufficiency. Vancomycin may NOT be active against *Staphyloccus haemolyticus* and *Staphylococcus epidermidis*.

Daptomycin (lipopeptide)

A cyclic lipopeptide active against **gram-positive organisms** including **vancomycin-resistant *Enterococcus*** and **methicillin-resistant staphylococci**. The drug of choice for MRSA when the MIC for vancomycin is > 2. It is ineffective for pulmonary infections because it is deactivated by surfactant. Can cause rhabdomyolysis; follow CPK Q week.

Metronidazole

A nitroimidazole with activity against **anaerobic bacteria** including ***C. difficile***, ***Bacteriodes fragilis***, and ***Peptostreptococcus***, and **protozoa** including ***Entamoeba histolytica, Girdia lamblia,*** and ***Trichomonas vaginalis.*** Subject to first-pass hepatic metabolism. Bioavailability is increased and clearance is decreased in cirrhosis.